

CONTROLLING REGIOSELECTIVITY OF CATALYTIC TRANSFER HYDROFUNCTIONALIZATION REACTIONS BY NON-COVALENT INTERACTIONS

INTRODUCTION

Catalysis revolutionized the synthesis of fine and bulk chemicals and is thus of crucial importance both in laboratory organic synthesis and in the chemical industry. It is estimated that catalysis is generally related to underpinning approximately 30% of global gross domestic product. Catalysis is involved at some point in the processing of over 80% of all manufactured products. By enabling new synthetic methods through creating new reaction paths, catalysts have improved the discovery and production of pharmaceuticals, agrochemicals, fertilizers, and other materials.

In recent years, one of the revolutionary concepts, namely shuttle catalysis has been introduced and explored. This strategy enables the formal transfer of small molecules (e.g., HCN, H₂/CO, HBr) between donor and acceptor molecules and thus can be utilized as a powerful synthetic tool for the functionalization of unsaturated molecules. Notably, transfer hydrofunctionalizations of alkenes (and alkynes) can be achieved with cheap, non-toxic, and easy to handle sacrificial donors, eliminating the necessity of direct utilization of toxic and hazardous gases (e.g., HCN, H₂/CO, HCl/CO) or specialized equipment, featuring strong benefit of this strategy. The shuttle hydrofunctionalizations would represent a widely applicable powerful tool for organic synthesis.

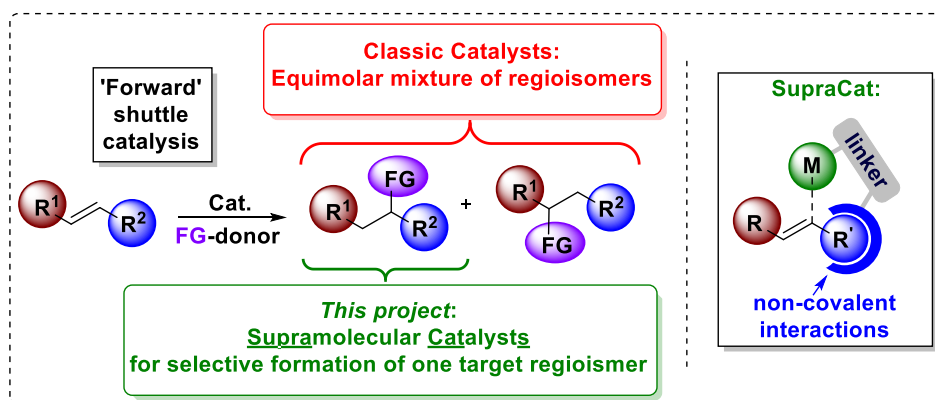


Figure 1. Supramolecular control of regioselectivity proposed in this project.

However, when unsymmetrical alkenes (or alkynes) are used in such transformations, mixtures of regioisomers are formed, irrespective of the type of transferred functional groups. (Fig. 1) This general limitation of shuttle hydrofunctionalization hampers the synthetic utility of the strategy, unless control of regioselectivity is achieved.

AIM OF THE PROJECT AND APPROACH

To address this issue, I postulate that new classes of precisely designed supramolecular catalysts (SupraCats) will selectively promote the formation of one target regioisomer (Fig. 1). Such catalysts will exploit additional non-covalent interactions to preorganize a substrate at the metal center to favor the formation of the target product (Fig. 1). Therefore, the strategy will precisely control the selectivity of reactions that are not conducted selectively with current methods. Consequently, this approach will provide access to a broad range of chemicals (e.g., nitriles, aldehydes, halides), the selective formation of which is currently limited but desired for both the development and production of fine chemicals and materials.

The detailed research program towards the general goal of the project is divided into three interplaying phases (P), related to: the design and synthesis of the SupraCats (P1), evaluation of the activity and selectivity of SupraCats (P2), scope, limitation and synthetic application of regioselective transfer hydrofunctionalizations (P3).

SIGNIFICANCE OF THE PROJECT RESULTS

The proposed research aims toward the development of a powerful strategy for selective catalysts, vastly increasing the range of utility of transfer hydrofunctionalizations, allowing access to target molecules, simplified syntheses with a reduced number of steps, reduction of waste generated, an increase of energetic and material efficiency. These aspects have great potential of applicability in other fields: easier synthesis of pharmaceuticals, simplifying the production of materials, reducing side reactions and contaminants, access to new materials from available precursors, development of environmental-friendly and energy-efficient industrial processes.